

rejected. Careful consideration has been given to the grounds for rejection, and the following discussion is offered in response. Reconsideration is respectfully requested.

REMARKS

The claims are directed to isolated STEAP-2 proteins defined by amino acid sequence or deposit. Dependent claims are directed to compositions for inducing an immunological response comprising these proteins. Of note, the claims are not directed to “immunotherapy of cancer” as asserted at page 3 of the Final Action (Paper 27).

As a preliminary matter, it will be noted that an immunological response includes inducing the production of antibodies and the antibodies raised may themselves be employed in various applications as will further be described below. Thus, the claims need not be limited to the use of STEAP-2 proteins as therapeutic vaccines, and the proteins themselves are useful in various ways.

Formal Matters

Applicants first note that the Revocation of Power of Attorney and Change of Address filed in regard to this case has apparently not been matched with the file and the Office action was sent to applicants’ previous representative. A copy of the Revocation of Power of Attorney and Change of Address, previously submitted, is included with this response.

Second, it is believed that the finality of the rejection is unjustified. The finality does not take account of the Declaration filed by Dr. Mary Faris in response to the prior final rejection. The Faris Declaration established physiological effects of the STEAP-2 protein when expressed in tumor cells. Although the Advisory Action indicates that the Declaration has been considered, no account has been taken of the demonstration of the properties of the STEAP-2 protein to impart drug resistance or to function as a calcium ion channel. These results, which are set forth in paragraphs 7-10 of that Declaration, were not addressed. Therefore, the following discussion will show the relevance of these results explicitly. Although applicants submit that all outstanding

rejections are moot, the proper Office response here is to withdraw the finality of any remaining rejection following consideration of the present submission.

The Rejections Under 35 U.S.C. § 112, First Paragraph

In rejecting the claims under this section, the Office refers to Paper 23; Paper 16, pages 3-5 and Paper 11, pages 6-11. In reviewing these Papers, several matters that are no longer pertinent are noticed:

First, it is that immunotherapy is not an issue here. Applicants are not required to demonstrate an immunotherapeutic response in order to show that the claimed subject matter is enabled with respect to how to make and use the invention. Further, the matter of fragments is no longer an issue; these are no longer claimed. Finally, the Office has acknowledged, in light of the previous Declaration of Dr. Mary Faris, that the claimed protein is actually produced in prostate tumors. Thus, the portions of these Actions which argue that it is unpredictable that the protein itself will be produced are moot as well.

Applicants believe that the issue, as now framed, is twofold:

- 1) whether the teaching that the claimed protein is an immunohistochemical and diagnostic target (the ability of the protein to do so has, rightfully, not been questioned) is a sufficient disclosure, and,
- 2) whether the claimed protein is itself useful as a screening tool in light of the ability of inhibitors of the activity associated with this protein to exert tumor retarding effects as is understood in the art.

An affirmative answer to even one of these is sufficient to meet the standards for patentability. Applicants submit that both are met. These issues are addressed by the enclosed Declarations.

The ability for an artisan to achieve immunohistochemical and diagnostic uses of STEAP-2 are addressed by the Declaration of Dr. Karen Morrison. The Morrison Declaration focuses on two applications for antibodies raised against STEAP-2.

First, these antibodies are useful in several aspects of diagnosis by immunohistochemical determinations of the localization or distribution of the STEAP-2 protein. These utilities are addressed, e.g., paragraphs 6-13 of Dr. Morrison's Declaration, alteration in the localization/distribution of a protein in a cell as detected by immunohistochemical methods, can be diagnostic for the presence of cancer, disease stage, progression and/or tumor aggressiveness, and these results also provide information concerning the favorability of treatment modalities - *e.g.*, the presence of the protein on the cell surface makes the cells more amenable to treatment with reagents (such as the antibodies themselves) that interact with the protein. Dr. Morrison's Declaration, in paragraphs 4-5, points out the support for such utilities in the specification as-filed.

Second, as pointed out by Dr. Morrison, the specification demonstrates that STEAP-2 is not present in many normal tissues. Figures 14 and 15 show this lack of expression in most normal tissues. Thus, any presence of STEAP-2 protein in these tissues, which normally lack it, would demonstrate the presence of metastases of tumors, as noted in paragraph 15 of Dr. Morrison's Declaration.

Based, then, on Dr. Morrison's Declaration alone, it is apparent that antibodies raised to the claimed protein are useful in immunohistochemical methods for making a diagnosis of cancer or non-malignancy, making prognostic indications, determining cancer progression, as well as in detection of metastases.

Also included with this response is a second Declaration by Dr. Mary Faris addressing STEAP-2 protein functions described in her previous Declaration, that STEAP-2 protein functions in calcium ion flux and in conferring drug resistance. As pointed out in paragraphs 4-5 of her present Declaration, the specification as-filed indicates that STEAP-2 functions as calcium ion

channel, and that it is known from various publications in the open literature that inhibition of calcium channel activity is an effective antitumor treatment. Therefore, the availability of the protein itself provides a valuable screening tool for compounds that will exhibit antitumor functions. In addition, it identifies STEAP-2 as a target for inhibition, thus indicating that antibodies raised with respect to STEAP-2 would themselves be useful in inhibiting its activity.

The desirability of inhibiting STEAP-2 protein function is further outlined in paragraphs 6-9 of Dr. Faris' Declaration. As was shown in Dr. Faris' Declaration filed previously, STEAP-2 protein functions in conferring drug resistance and this is further verified in the present Declaration. Clearly inhibitors of this protein, including antibodies directed to it, would be useful in restoring drug sensitivity to these cells.

As noted in paragraph 9 of the Faris Declaration, it is useful to diagnose that STEAP-2 protein is present in a tumor. Diagnostic uses of STEAP-2 are extensively addressed in the Morrison Declaration. Accordingly, STEAP-2 protein and antibodies directed thereto are useful in various diagnostic applications.

In summary, the enclosed Declarations provide more than adequate evidence that the claimed protein and antibodies immunospecific therefor may be used as described in the specification for diagnosis and treatment of prostate tumors. A use need be limited to immunotherapy, and diagnostic conclusions are made not merely on the simple presence of the protein in a cell, but also on cell's immunohistochemical characteristics as well as where such cells occur in the body. Further, the protein itself is useful as a screening tool in view of its demonstrated tumor enhancing and drug resistance conferring activities.

In view of this evidence, supported originally in the specification at the locations noted in the Declarations, withdrawal of the rejection under 35 U.S.C. § 112, paragraph 1, is believed proper. Accordingly, applicants respectfully request claims 1 and 44-48 be passed to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 511582001620.

Respectfully submitted,

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